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AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claims 1-143 (canceled).

Claim 144 (currently amended): A method of regulating expression of a desired protein or RNA in a non-human transgenic animal *in vivo*, the method comprising:

administering to the transgenic animal a pharmacological dose of a ligand, which is an antagonist for a non-mutated steroid hormone receptor protein, wherein the transgenic animal comprises:

- (a) a nucleic acid encoding a molecular switch comprising a mutated receptor protein, wherein the mutated receptor protein comprises:
 - (i) a non-steroid hormone receptor DNA binding domain which binds a promoter that is transcriptionally linked to a target gene;
 - (ii) a mutated progesterone receptor ligand binding domain which is distinct from a naturally occurring ligand binding domain by deletion of up to 54 ~~naturally occurring carboxyl~~ authentic carboxy terminal amino acids of the ligand binding domain, thereby reversing ligand specificity of the receptor and conferring activation by the antagonist; and
 - (iii) a transactivation domain which causes a transcription from the promoter when the molecular switch is bound to the promoter and the ligand; and
- (b) a target gene transcriptionally linked to the promoter, wherein the nucleic acid encoding the molecular switch protein is expressed in the transgenic animal and administration of the ligand results in binding of the molecular switch protein to the promoter thereby regulating expression from the target gene.

Claim 145-146 (cancelled)

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Claim 147 (previously presented): The method of claim 144, wherein the target gene and promoter are encoded on a nucleic acid cassette that has been introduced into the transgenic animal.

Claim 148 (previously presented): The method of claim 144, wherein the non-steroid hormone receptor DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or, a modified DNA binding domain.

Claim 149 (cancelled)

Claim 150 (previously presented): The method of claim 144, wherein the nucleic acid encoding the molecular switch has been introduced into the transgenic animal on an expression vector that encodes the molecular switch.

Claim 151 (previously presented): The method of claim 144, wherein the DNA binding domain is a Gal-4 DNA binding domain.

Claim 152 (previously presented): The method of claim 144, wherein the mutated ligand binding domain binds a compound selected from the group consisting of 5 α -pregnane-3, 20-dione; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -propinyl-4, 9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 α -hydroxy-17 β -(3-hydroxypropyl)-13 α -methyl-4,9-gonadiene-3-one; 11 β -(4-acetylphenyl)-17 β -hydroxy-17 α -(1-propinyl)-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -(3-hydroxy-1 (Z)-propenyl-estra-4, 9-diene-3-one; (7 β ,11 β ,17 β)-11-(4-dimethylaminophenyl)-7-methyl-4', 5'-dihydrospiro(ester-4, 9-diene-17, 2'(3'H)-furan)-3-one; (11 β ,14 β ,17 α)-4',5'-dihydro-11-(4-dimethylaminophenyl)-(spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.

Claim 153 (previously presented): The method of claim 144, wherein the mutated progesterone receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.

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Claim 154 (previously presented): The method of claim 144, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

Claim 155 (previously presented): The method of claim 144, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.

Claim 156 (previously presented): The method of claim 155, wherein the transactivation domain comprises a TAF-1 transactivation domain.

Claim 157 (previously presented): The method of claim 155, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.

Claim 158 (previously presented): The method of claim 155, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.

Claim 159 (previously presented): The method of claim 144, wherein the molecular switch is tissue specific.

Claim 160 (previously presented): The method of claim 159, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

Claim 161 (previously presented): The method of claim 147, wherein the target gene and promoter are encoded in a nucleic acid cassette that further comprises a tissue-specific cis-element.

Claim 162 (cancelled):

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Claim 163 (previously presented): The method of claim 144, wherein the ligand is RU38486.

Claim 164 (previously presented): The method of claim 144, wherein the ligand is 11 beta-(4-dimethylaminophenyl)-17 beta-hydroxy-17 alpha-propinyl-4, 9-estradiene-3-one.

Claim 165 (previously presented): The method of claim 144, wherein the ligand is an antiprogestrone.

Claim 166 (previously presented): The method of claim 144, wherein the ligand requires conversion to an active form in an end organ.

Claim 167 (previously presented): The method of claim 144, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.

Claim 168 (currently amended): A method of regulating expression of a target gene in an animal *in vivo* comprising:

administering to the animal a pharmacological dose of a ligand that activates a molecular switch encoded by a molecular switch expression cassette, the cassette having been previously administered to the animal for transient expression, wherein the molecular switch comprises

- (i) a sequence specific non-steroid hormone receptor DNA binding domain;
- (ii) a mutated progesterone receptor ligand binding domain which is distinct from a naturally occurring ligand binding domain by deletion of up to 54 ~~naturally occurring carboxyl~~ authentic carboxy terminal amino acids of the ligand binding domain, said mutated ligand binding domain is activated by the ligand which is not a native ligand for the corresponding wild type progesterone receptor; and
- (iii) a transregulatory domain, wherein the molecular switch is expressed in the animal and the activation of the molecular switch by the ligand results in binding to a specific DNA sequence in the regulatory region of a target gene promoter and expression from the target gene.

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Claim 169 (cancelled)

Claim 170 (previously presented): The method of claim 168, wherein the ligand is an anti-progestin.

Claim 171 (previously presented): The method of claim 170, wherein the anti-progestin is selected from the group consisting of: RU 38486; Org31806; and Org 31376.

Claim 172 (canceled)

Claim 173 (previously presented): The method of claim 168, wherein the DNA binding domain is selected from the group consisting of: a GAL-4 DNA binding domain; a viral DNA binding domain; an insect DNA binding domain; and a non-mammalian DNA binding domains.

Claim 174 (previously presented): The method of claim 168, wherein the molecular switch further comprises a transactivation domain distinct from a steroid hormone receptor superfamily transactivation domain.

Claim 175 (previously presented): The method of claim 168, wherein the target gene expression is up-regulated.

Claim 176 (previously presented): The method of claim 168, wherein the target gene expression is down-regulated.

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Claim 177 (currently amended): A method of regulating a transient expression of a desired protein or RNA in an animal *in vivo*, the method comprising:

administering to the animal a pharmacological dose of a ligand, which is an antagonist for a non-mutated progesterone receptor protein, wherein the animal has been previously administered a coding sequence of a molecular switch comprising a mutated progesterone receptor protein and expresses the molecular switch, wherein the mutated progesterone receptor protein comprises:

- (i) a DNA binding domain specific for a DNA site on a promoter that is transcriptionally linked to a target gene comprised in the animal;
- (ii) a mutated progesterone receptor ligand binding domain which is distinct from a naturally occurring ligand binding domain by deletion of up to 54 ~~naturally occurring carboxyl~~ authentic carboxy terminal amino acids of the ligand binding domain, said mutated ligand binding domain is activated by the ligand; and
- (iii) a transactivation domain which causes a transcription from the promoter when the molecular switch is bound to the promoter and the ligand, wherein administration of the ligand results in binding of the molecular switch to the promoter and thereby regulates expression of the desired protein or RNA from the target gene.

Claim 178 (previously presented): The method of claim 177, wherein the DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or a modified DNA binding domain.

Claim 179 (previously presented): The method of claim 177, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

Claim 180 (previously presented): The method of claim 177, wherein the animal is a mammal.

Claim 181 (previously presented): The method of claim 180, wherein the mammal is a human.

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Claim 182 (previously presented): The method of claim 177, wherein the ligand selected from the group consisting of 5 α -pregnane-3,20-dione; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -propinyl-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 α -hydroxy-17 β -(3-hydroxypropyl)-13 α -methyl-4,9-gonadiene-3-one; 11 β -(4-acetylphenyl)-17 β -hydroxy-17 α -(1-propinyl)-4,9-estradiene-3-one; 11 β -(4-dimethylaminophenyl)-17 β -hydroxy-17 α -(3-hydroxy-1(Z)-propenyl)-estra-4,9-diene-3-one; (7 β ,11 β ,17 β)-11-(4-dimethylaminophenyl)-7-methyl-4',5'-dihydrospiro(ester-4,9-diene-17,2'(3'H)-furan)-3-one; (11 β ,14 β ,17 α)-4',5'-dihydro-11-(4-dimethylaminophenyl)- (spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.

Claim 183 (previously presented): The method of claim 177 wherein the ligand is an anti-progesterone.

Claim 184 (previously presented): The method of claim 183 wherein the antiprogesterone is RU 34846, Org 31806, or Org 31376.

Claim 185 (previously presented): The method of claim 177, wherein the mutated progesterone receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.

Claim 186 (previously presented): The method of claim 177, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.

Claim 187 (previously presented): The method of claim 177, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.

Claim 188 (previously presented): The method of claim 177, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.

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Claim 189 (previously presented): The method of claim 177, wherein the molecular switch is tissue specific.

Claim 190 (previously presented): The method of claim 189, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

Claim 191 (previously presented): The method of claim 190, wherein the target gene further comprises a tissue-specific cis-element.

Claim 192 (previously presented): The method of claim 177, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.